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FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
COOK, LISA V	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/814,125
Filing Date: April 01, 2004
Appellant(s): FROSTEGARD, JOHAN

Steven L. Highlander
Reg. No. 37,642
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12 September 2007 appealing from the Office action mailed 7 March 2007.

(1) Real Party in Interest

A statement identifying, Athera Biotechnologies, AB Stockholm Sweden, by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. Appendix A filed 9/12/07 in the Appeal Brief does not include canceled claim number 15. A correct statement of the status of the claims is as follows:

A. This appeal involves claims 1-14 and 16-26.

B. Claim 15 has been canceled.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner because the Terminal Disclaimer filed 12/5/06 has been approved.

A. Claims 1-13 as allegedly obvious over the claims of U.S. Patent 6,780,605 (Exhibit 1) in view of Muzya et al. (Exhibit 2).

B. Claims 14 and 16-26 as allegedly obvious over the claims of U.S. Patent 6,780,605 (Exhibit 1) in view of Muzya et al. (Exhibit 2) and Baldo et al. (Exhibit 3).

(7) Claims Appendix

A substantially correct copy of appealed claims appears on page 9 and 10 of the Appendix to the appellant's brief. The minor errors are as follows: Canceled claim 15 was not included.

(8) Evidence Relied Upon

A. Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06).

B. Ostermann et al. (Thrombosis Research, 52, 529-540, 1988).

C. Barquinero et al. (Lupus, 1994, 3, 55-58).

D. Smal et al. (Journal of Immunological Methods, Vol.128, 1990, pages 183-188).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Objections

A. Claims 21-26 are objected to because of the following informalities: phosphochline is misspelled. The term should be spelled "phosphocholine".

Claim Rejections - 35 USC § 103

B. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 1-3, 6-8, 11-14, 16-17, 20-23, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988).

Muzya et al. teach that antibodies involving that bind to PAF, lyso-PAF, and acyl analogs of PAF. The binding of antiphosphatidylcholine antibodies to PAF and its structural analogs is related to the presence of phosphocholine fragments. The binding of antiphosphatidylcholine antibodies to PAF was exemplified in the sera of women with obstetrical-gynecological disorders (reading on spontaneous abortions). See abstract.

In particular, Muzya et al. teach an enzyme immunoassay (EIA) to study the binding of antibodies that bind to PAF and its structural analogues. In the assay PAF (a type of phosphocholine as exemplified in the specification on page 14 lines 12-11) was placed on polystyrene microplates.

The assay procedure also includes a reagent for detecting the antibodies bound to PAF (conjugates of murine monoclonal antibody with horseradish peroxidase IgM and IgG). See page 11, 2nd paragraph. The reagents are employed to measure PAF – antibody binding in blood serum test samples. The serum from a patient with late toxicosis in pregnancy had a high level of IgG antibodies that were reactive with PAF. The patient's serum bound significantly less to a PAF analogues. The researches taught that this may be caused by specific antibodies to PAF.

Although Muzya et al. teach the reagents and methods required by the claims; they do not specifically teach the diagnosis of risk of cardiovascular disease comprising atherosclerosis. In other words, Muzya et al. differ from the instant invention in not specifically teaching PAF as an

indicator for cardiovascular diseases such as atherosclerosis via PAF quantification in serum and plasma.

However, Ostermann et al. teach PAF quantification in serum and plasma as well as its correlation/diagnosis (discrimination) in Atherosclerotic patients. See abstract and page 531 2nd paragraph. Thirty-Six health volunteers and 40 atherosclerotic patients were evaluated in the study. Blood samples were analyzed to determine PAF concentration.

The results showed a significant increase in serum PAF levels of patients suffering from coronary artery disease. Page 536, last paragraph. The researchers also measured plasma levels. See page 538.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure PAF concentrations in serum and plasma patients with cardiovascular disease such as atherosclerosis as taught by Ostermann et al. in the method of Muzya et al. because Ostermann et al. teach the critical role of PAF in myocardial infarction/atherosclerosis and its accuracy of correctly classifying subjects. See abstract. Ostermann et al. further teach that PAF could discriminate between low and high-risk groups and was an improvement over other commonly utilized discriminators (total cholesterol, VLDL/LDL-cholesterol, apo). See page 537 2nd paragraph.

One having ordinary skill in the art would have been motivated to do this because the early detection of such disorders is both beneficial in possible prevention and treatment of the disease.

II. Claims 4, 9, 18, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988) and further in view of Barquinero et al. (Lupus, 1994, 3, 55-58).

Please see Muzya et al. in view of Ostermann et al.

Muzya et al. in view of Ostermann et al. differ from the instant invention in not specifically teaching assay measurements by enzyme-linked immunoassay.

However, Barquinero et al. teach an ELISA assay to measure antibodies against platelet-activating factor (PAF) in patients with autoimmune diseases. Specifically blood sample from patients with SLE (systemic lupus crythematosus), PAPS (antiphospholip syndrome), and syphilis. PAF was shown to be significantly present in patients with syphilis. See abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the reagents taught by Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11) in view of Ostermann et al. in an enzyme linked immunoassay (ELISA) as taught by Barquinero et al. (Lupus, 1994, 3, 55-58) because Barquinero et al. taught that the PAF ELISA could be used to detect syphilis. See Barquinero et al. abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF".

III. Claims 5, 10, 19, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-

092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988) and further in view of Smal et al. (Journal of Immunological Methods, Vol.128, 1990, pages 183-188).

Please see Muzya et al. in view of Ostermann et al.

Muzya et al. in view of Ostermann et al. differ from the instant invention in not specifically teaching assay measurements by radioimmunoassay.

However, Smal et al. teaches method to evaluate PAF in a specific and sensitive radioimmunoassay. In the procedure the anti-PAF antibodies showed specificity for the acetyl group at the C2 position of the PAF molecule and exhibited no significant cross-reactivity with lyso-PAF or the naturally occurring lipids. The RIA was at least as good as the platelet-based assay for PAF but the RIA was simpler to perform, had higher capacity and did not have the draw backs of the inherent variability associated with the bioassay. See abstract and pages 186-187.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to take the reagents taught by Muzya et al. in view Ostermann et al. to measure PAF by radioimmunoassay procedures as exemplified by Smal et al. because Smal et al. taught that the RIA was at least as good as the platelet-based assay for PAF but the RIA was simpler to perform, had higher capacity and did not have the draw backs of the inherent variability associated with the bioassay. See abstract and pages 186-187.

(10) Response to Argument

The arguments against the rejection for alleged obviousness-type double patenting is MOOT, because the rejections have been withdrawn.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that Muzya et al. is cited as teaching that antibodies bind to PAF, lyso-PAF, and acyl analogs of PAF while Ostermann is cited as teaching PAF quantification in serum and plasma as well as correlation/diagnosis with atherosclerosis. This argument has been carefully considered but not found persuasive because Muzya et al. also teaches blood serum sampling see page 3 1st and 2nd paragraphs, wherein "blood serum samples taken in the Scientific Centre of Obstetrics,….." and EIA procedures utilizing blood serum test samples. The reference to Ostermann was merely employed to establish the relationship between PAF/antibodies to PAF complex measurements and early cardiovascular disease.

While a deficiency in a reference may overcome a rejection under 35 USC §103, a reference is not overcome by pointing out that a reference lacks a teaching for which other references are relied. In re Lyons, 364 F.2d 1005, 150 USPQ 741, 746 (CCPA 1966).

Applicant contends that the instant invention is not examining PAF content in serum or plasma but rather *antibodies* to PAF or *antibodies* to PAF derivatives. This argument was carefully considered but not found persuasive because the claims are drawn to not only the concentration of the antibody bound to PAF but the presence of said antibodies bound to PAF. See claim 1. Thus the claims do not simply require the measurement of the antibodies bound to PAF but also read on effects detected by the mere presence of the complex formed (antibodies to PAF bound to PAF).

More Specifically, the rejection under 35 USC §103 over Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Collective of Authors, 1997 UDC 618.3-092:812.087.1]-078-33, submitted by applicant on 12/5/06) in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988) teaches the same procedures. PAF (platelet–activating factor or 1-O-alkyl-2-o-acetyl-sn-glycerol-3-phosphocholine, see Ostermann, Vol.52, No.6, page 530) is added to a sample of biological fluid and the interaction of the PAF with antibodies present in the sample is measured. See Muzya et al. page 4 2nd paragraph and Ostermann 531 (PAF-degrading capacity).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., only the measurement of the concentration of antibodies to PAF) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that Muzya examines anti-PAF antibodies but only addresses gynecological disorders. Examiner agrees and notes that Ostermann was combined with Muzya to make obvious the relationship between early cardiovascular disease and the complex formed between PAF and antibodies to PAF.

Applicant argues that Ostermann says nothing about PAF levels or anti-PAF antibody levels in subjects. This argument was carefully considered but not found persuasive because Ostermann was not relied on for that teaching. In addition, Ostermann teaches a method of adding ^{14}C-PAF (Applicant's phosphocholine) to serum samples (page 531) and measuring the interaction of PAF bound to antibodies to PAF (Table 1-3). Ostermann teaches that the mean

PAF-degrading capacity of serum from myocardial infarction survivors was found to be significantly increased in comparison with that of controls. See page 533 last two paragraphs.

The test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one or ordinary skill in the pertinent Art. See In re Bent, 52 CCPA 850, 144 USPQ 28 (1964), In re Nievelt, 179 USPQ 224 (CCPA 1973).

Specifically Muzya et al. teach the detection of anti-PAF antibodies. While Ostermann et al. teach that the mean PAF-degrading capacity of serum from myocardial infarction survivors were found to be significantly increased in comparison to control serum samples. See page 533 last two paragraphs. PAF is further taught to play a role in the development of atherosclerosis (an early cardiovascular disease assessor). See page 536 discussion, for example.

Further, Applicant contends that Ostermann assay for PAF aceythydrolase activity. However, regardless of the method of measurement taught by Ostermann the relationship between early cardiovascular disease and PAF/antibodies bound to PAF is clearly identified.

Applicants contend that the reference of Barquinero et al. does not teach a correlation between anti-PAF antibodies and autoimmune disease. In fact, Barquinero provides a link between anti-PAF antibodies and syphilis. Barquinero has been cited to merely teach ELISA procedures for measuring PAF/anti-PAF binding procedures. This argument was carefully considered but not found persuasive because there is no requirement that the prior art must suggest that the claimed invention will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. *In re Dillon*, 919 F.2d 688, 696, 16 USPQ 2d 1897, 1904 (Fed. Cir. 1990).

Applicant argues that Barquinero et al. and Smal et al. cannot rescue the deficiencies of the primary references and should be withdrawn. The primary references have been addressed a priori and have been maintained. Accordingly the rejections including Barquinero et al. and Smal et al. have been maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Lisa V. Cook/
Examiner, Art Unit 1641

Conferees:

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641

/Robert A. Wax/
Robert A. Wax
TQAS Appeals Specialist
Technology Center 1600